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EXAMINER	
RAO, DEEPAK R	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 11/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/770,382	PATEK ET AL.	
	Examiner	Art Unit	
	Deepak Rao	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-76* is/are pending in the application.

4a) Of the above claim(s) *10,11,51,59 and 60* is/are withdrawn from consideration.

5)☒ Claim(s) *62* is/are allowed.

6)☒ Claim(s) *1-9,12-50,52-58 and 62-76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20041213*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-76 are pending in this application.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-9, 12-50, 52-58, 61-75 and 76 in the reply filed on August 18, 2006 is acknowledged. The traversal is on the ground(s) that the restriction is improper because there is no serious burden. This is not found persuasive because the compounds of Groups I-VI are structurally dissimilar and are not art recognized equivalents. They are structurally dissimilar such that a reference anticipating a compound of Group I may not render the compounds of Groups II-VI obvious or vice-versa. 37 CFR 1.141(a) provides that two or more independent and distinct inventions may not be claimed in one application, whether or not the misjoinder occurred in one claim or more than one claim. Restriction is going to be exercised where independent and distinct inventions are presented in one Markush grouping. Independent means when the compound is being made and/or used alone, not in combination with other compounds of the Markush expression. Restriction is considered proper in Markush claims where the members are so diverse and unrelated that a prior art reference anticipating the claim with respect to one of the members, would not render the claims obvious under 35 U.S.C. 103 with respect to the other members. Therefore, what should be considered for patentable distinctness is the compound as a whole. Each of the groups is classified separately and further, the compounds of Groups I-VI require separate searches in patent and literature databases and therefore, it is burdensome for the examiner.

The requirement is still deemed proper and is therefore made FINAL.

Claims 10-11, 51 and 59-60 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention(s), there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on August 18, 2006.

Applicant's election of the species of Example 96 is also acknowledged. As the elected species was not found in the prior art, the search was expanded to the elected invention of Group I, compounds of formula (I) wherein p is 0 and R2 and R3 are independent substituents and are NOT taken together to form a cyclic group.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 63-75 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a patient suffering from rheumatoid arthritis, does not reasonably provide enablement for a method for inhibiting the activity of protein kinase generally or a method for treating a patient suffering from or subject to a physiological condition that can be ameliorated by the administration of a protein kinase inhibitor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed. The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations.

The instant claim 63 is drawn to 'a method of inhibiting the activity of a protein kinase' and the dependent claims 65-68 provide some specific protein kinases: EGFR, Fak, ... KDR, PLK, ... Raf. The specification does not provide any test procedures to measure the VEGFR, KDR, EGFR, PLK, FLK-1, etc. protein kinase inhibition activity. The specification merely recites that the compounds are useful as protein kinase inhibitors and based on the kinase inhibition activity, the specification provides that the compounds are useful in the treatment of a physiological condition that can be ameliorated by the administration of protein kinase inhibitors. The disclosure and the claims further provides a wide variety of diseases or conditions that fall within the scope of the instant claims - such as disorders of blood vessel proliferation, fibrotic disorders, ... metabolic disorders, ... diseases of the nervous system, ... oncology diseases and cancer. The instant claims appear to be 'reach through' claims. Reach through claims, in general have a format drawn to mechanistic, receptor binding or enzymatic functionality and thereby reach through any or all diseases, disorders or conditions, for which they lack

written description and enabling disclosure in the specification thereby requiring undue experimentation for one of skill in the art to practice the invention.

The specification does not provide any guidance to test the instantly claimed 'protein kinase inhibition' activity. The recitation "protein kinase" encompasses all members of the protein kinase super family. The specification does not provide the sources for the various enzymes encompassed by the instant claims, e.g., VEGF, KDR, EGFR, etc. There is neither data to if any of the compounds were tested or not; nor data on which enzymes were inhibited and which ones were not. Applicant did not state on record or provide any guidance that which state of the art assays may provide basis for the instantly claimed activity. Further, there is no disclosure regarding how this potential inhibitory activity is correlated to the clinical efficacy of the treatment of various disorders of the claims. As can be seen from specification page 53, data related to the protein kinase inhibition holds significant role in determining the dosage regimen based on the minimal effective concentration of each of the compound to achieve the desired inhibition of the protein kinases.

The instant claims are drawn to "a method for treating a patient suffering from or subject to a physiological conditions that can be ameliorated by the administration of a protein kinase inhibitor" including diseases of the nervous system, oncology diseases, cancer, etc." First, the instant claims cover 'diseases' that are known to exist and those that may be discovered in the future, for which there is no enablement provided. The use disclosed in the specification is as protein kinase inhibitors, in the treatment of a laundry list of diseases, which include cancer, diseases of the nervous system, etc. There are no test assays and procedures provided in the specification and there is nothing in the

disclosure regarding how this recited activity correlates to the treatment of the diverse disorders of the instant claims. The diseases and disorders encompassed by the instant claims include various types of cancer, diseases of the nervous system, etc., some of which have been proven to be extremely difficult to treat. Further, there is no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same. Note *In re Surrey*, 151 USPQ 724 regarding sufficiency of disclosure for a Markush group.

Further, the instant claims recite treating of diseases mediated by various types of protein kinases, and there is no disclosure regarding how all these assorted types diseases are treated. See MPEP § 2164.03 for enablement requirements in cases directed to structure-specific arts such as the pharmaceutical art. Receptor activity is generally unpredictable and highly structure specific area, as evidenced by the wide range of results obtained for the tested compounds. It is inconceivable as to how the claimed compounds can treat the large list of diseases embraced by the claims having diverse mechanisms or inhibit protein kinases generally. Further, there is no disclosure regarding how the patient in need of the treatment requiring the specific kinase (i.e., VEGFR, KDR, EGFR, AKT, etc.) inhibiting activity is identified and further, how all types of the diseases having divers mechanisms are treated. The state of the art is indicative of the unpredictability of the therapeutic approach based on kinase inhibiting activity. Cressey et al. (Medline Abstract 2005) state that "Although numerous publications dealing with the measurement of circulating VEGF for diagnostic and therapeutic monitoring have

been published, the relationship between the production of tissue VEGF and its concentration in blood is still unclear".

The instant claims include 'a method for treating oncology diseases and cancer in a patient suffering from or subject to'. The terms 'cancer' and 'oncology diseases' represent anything that is caused by abnormal tissue growth. That can be growth by cellular proliferation more rapidly than normal, or continued growth after the stimulus that initiated the new growth has ceased, or lack (partial or complete) of structural organization and/or coordination with surrounding tissue. It can be benign or malignant. Thus, such term covers not only all cancers, but also covers precancerous conditions such as lumps, lesions, polyps, etc. No compound has ever been found to treat cancers of all types generally. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a "silver bullet" is contrary to our present understanding of oncology. For example, Yano et al. (Medline Abstract 2000) provides for the treatment of malignant pleural effusion of human lung adenocarcinoma by inhibition of VEGF receptor, however, the state of the art is not indicative any pharmaceutical agents that are useful in the treatment or prevention of cancer generally. Cecil Textbook of Medicine states that "each specific type has unique biologic and clinical features that must be appreciated for proper diagnosis, treatment and study" (see the enclosed article, page 1004). Different types of cancers affect different organs and have different methods of growth and harm to the body. Also see *In re Buting*, 163 USPQ 689 (CCPA 1969), wherein 'evidence involving a single compound and two types of cancer, was held insufficient to establish the utility of the claims directed to disparate types of cancers'. Thus, it is beyond the skill of

oncologists today to get an agent to be effective against cancers generally. In reference to cancer treatment using protein tyrosine kinase inhibitors, Traxler (Exp. Opin. Ther. Patents, 1997) stated that "pharmacological properties such as stability in biological media, bioavailability, metabolism or formulability are significant hurdles" see page 585, col. 2, lines 33-36. Fabbro et al. (Pharmacology & Therapeutics, 2002) regarding 'Protein kinases as targets for anticancer agents' indicate that: "key to the discovery of new therapeutic anticancer approaches is the selection of epidemio-logically relevant, susceptible protein kinase targets, coupled with efficient searches for lead drug candidates and optimization of these lead molecules for potency, selectivity, efficacy and biopharmaceutical properties" (see page 95).

The claims recite the use of the instantly claimed compounds in treating 'disorders of blood vessel proliferation' which includes vascularization of a tissue involving the development of new capillary blood vessels, wherein some of these are not seen as being a disease or disorder, but as an absolutely essential body process. Thus, there is no enablement for treating something which is not itself a problem and is indeed essential for life.

The claims include 'a method for treating a patient suffering from or subject to disorders of the nervous system', which cover diverse disorders such as Alzheimer's disease, dementia, hereditary cerebellar ataxias, paraplegias, syringomyelia, phakomatoses, and much more. In fact, Layzer, Cecil Textbook of Medicine (article enclosed), states that 'some degenerative diseases are difficult to classify because they involve multiple anatomic locations' (see page 2050). For example, Alzheimer's disease has traditionally been very difficult or impossible to prevent or even to treat effectively

with chemotherapeutic agents. See e.g., the Cecil Textbook of Medicine, 20th edition (1996), Vol. 2, wherein it is stated that '[t]here is no cure for Alzheimer's disease, and no drug tried so far can alter the progress of the disease' (pg. 1994).

The diagnosis of each of the disease is generally suggested by medical history and reports of endoscopy, cytology, X-ray, biopsy, etc. depending on the symptoms, signs and complications, which is essential to establish the dosage regimen for appropriate treatment or prevention. The disclosure does not provide any guidance towards the dosage regimen required to facilitate the treatment and/or inhibition of the claimed disorders, nor indicate competent technical references in the appropriate methods.

Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Traxler, in a recent article (Exp. Opin. Ther. Patents, 1997) stated that "The concept of the inhibition of growth factor receptor-mediated signal transduction via inhibition of its protein tyrosine kinase is a novel, **not yet proven** clinical approach to the regulation of cell proliferation", see page 585, col. 1. Therefore, the state of the art provides the need of undue experimentation for the instantly claimed therapeutic benefits.

(Only a few of the claimed diseases are discussed here to make the point of an insufficient disclosure, it does not definitely mean that the other diseases meet the enablement requirements).

The instant claims are also drawn to 'a method for treating a patient **subject to** the physiological conditions' and therefore, the instant claim language appears to include 'prevention' of the recited disorders in a patient, which is not remotely enabled. 'To prevent' actually means *to anticipate* or *counter in advance, to keep from happening etc.* (as per Websters II Dictionary) and therefore it is not understood how one skilled in the art can reasonably establish the basis and the type of subject to which the instant compounds can be administered in order to have the "preventive" effect. It is inconceivable from the *in vitro* data of a small number of representative compounds can be correlated to the 'treatment and prevention' of the conditions recited in the claims, such that the claimed compounds can not only treat but also "prevent" the disorders or conditions of the instant claims. Further, there is no evidence on record which demonstrates that the *in-vitro* screening test relied upon is recognized in the art as being reasonably predictive of success in any of the contemplated areas of 'prevention'. Such a reasonable correlation is necessary to demonstrate such utilities. See *Ex parte Stevens*, 16 USPQ 2d 1379 (BPAI 1990); *Ex parte Busse et al.*, 1 USPQ 2d 1908 (BPAI 1986) (the evidence must be accepted as "showing" such utility, and not "warranting further study").

MPEP § 2164.01(a) states that "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)". That conclusion is clearly justified here and undue experimentation will be required to practice the claimed

invention.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the use of the invention. In view of the breadth of the claim, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9, 12-50, 52-58, and 62-76 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

1. In claim 1, in proviso statement a), it is recited that "Y and Y1, which may be identical or different, are at least one is –OCF3 or –S-**alk**" wherein it is not clear what is intended by the term "**alk**". The claims also recite another term "-SO_2**Alk**" (see e.g., proviso d). The terms "alk" or "Alk" are not standard abbreviations having a definite meaning. (This applies to all occurrences of the above term throughout the claims).
2. Claim 1 recites the limitation "then R2 and R3 are not one hydrogen and the other imidazolylalkyl" in proviso statement a) (see page 15, line 18). There is insufficient antecedent basis for this limitation in the claim because the definition

of R2 and R3 (on page 13, lines 6-13) does not include the term 'imidazolylalkyl' or recites a term which encompasses 'imidazolylalkyl'. It is not understood how a definition can be excluded from the claim without first including the term in the claim. (This applies to all occurrences of the above term throughout the claims).

3. Claim 1 recites the limitation "then R2 and R3 are not one hydrogen and the other alkyl optionally interrupted with O, S or N-alk" in proviso statement a) (see page 15, line 21-22). There is insufficient antecedent basis for this limitation in the claim because the definition of R2 and R3 (on page 13, lines 6-13) does not include the recitation 'alkyl optionally interrupted with O, S or N-alk'. The definition of R2 and R3 in claim 1 includes 'alkyl', however, it is not recited in the definition that the alkyl can be 'optionally interrupted by O, S or N-alk'. It is not understood how a definition can be excluded from the claim without first including the term in the claim. (This applies to all occurrences of the above term throughout the claims).

4. In claim 1, proviso statement b), the recitation "R2 and R3 are not one hydrogen and the other alkyl optionally interrupted by O, S or N-alk**; always substituted with a hydroxamate (-CO-NHOH)**", wherein it is not understood what is intended by the recitation 'always substituted with a hydroxamate (-CO-NHOH)'. The above recitation stands by itself following a semicolon (;) and it is not clear which group is referred as being 'always substituted'.

5. Claim 1 recites the limitation "always substituted with a hydroxamate (-CO-NHOH)" in proviso statement b) (see page 15, line 18). There is insufficient antecedent basis for this limitation in the claim because none of the variable

definitions positively identify "hydroxamate (-CO-NHOH)" as a substituent on any of the groups. It is not understood how a definition can be excluded from the claim without first including the term in the claim. (This applies to all occurrences of the above term throughout the claims).

6. Claim 1 recites the limitation "then R2 and R3 are not selected from the group consisting of hydrogen, alkyl, **arylalkyl**, aryl and heteroaryl" in proviso statement c) (see page 15, line 18). There is insufficient antecedent basis for this limitation in the claim because the definition of R2 and R3 (on page 13, lines 6-13) does not include the term 'arylalkyl'. It is not understood how a definition can be excluded from the claim without first including the term in the claim. (This applies to all occurrences of the above term throughout the claims).

7. Claim 6 recites the limitation "Y and Y1, which may be identical or different, are at least one is **$-OCF_3$**, ..." in proviso statement a) (see page 21, lines 4-5). There is insufficient antecedent basis for this limitation in the claim because the definition provided for Y and Y1 at lines 2-3 of the claim does not include the term "$-OCF_3$". It is not understood how a definition can be excluded from the claim without first including the term in the claim.

8. Claim 6 recites the limitation "Y and Y1, which may be identical or different, are at least one is **$-S(O)_n$-alk**, ..." in proviso statement b) (see page 21, lines 8-9). There is insufficient antecedent basis for this limitation in the claim because the definition provided for Y and Y1 at lines 2-3 of the claim does not include the term "**$-S(O)_n$-alk**". It is not understood how a definition can be excluded from the claim without first including the term in the claim.

9. Claim 8 recites the limitation "all the alkyl, alkenyl, ... or heteroaryl are optionally substituted with one or more radicals, which may be identical or different, chosen from halogen, cyano, ... **carboxyl which is free, salified, esterified with an alkyl radical or amidated with –NR11aR12a**" in lines 4-5. There is insufficient antecedent basis for this limitation in claim 1, see the recitation in claim 1 (page 14, lines 22-28) regarding the further substituents on the groups 'carbocyclyl, ... alkyl, alkenyl, ...' (provided below), which does not include a definition consistent with the above recitation. because the definition of R2 and R3 (on page 13, lines 6-13) does not include the term 'arylalkyl'.

> all the carbocyclyl, heterocyclyl, alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, heterocyclyl, aryl and heteroaryl above, and also the ring formed by R5 and R6 with the nitrogen atom to which they are attached, are optionally substituted with one or more substituents, which may be identical or different, selected from the group consisting of halogen, cyano, hydroxyl, alkoxy, $-CF_3$, nitro, aryl, heteroaryl, -C(=O)-OR9, -C(=O)-R8, -NR11R12, -C(=O)-NR11R12, -N(R10)-C(=O)-R8, -N(R10)-C(=O)-OR9, -N(R10)-C(=O)-NR11R12, -N(R10)-S(O)$_n$-R8, -S(O)$_n$-R8, -N(R10)-S(O)$_n$-NR11R12 and -S(O)$_n$-NR11R12,

10. In claim 8, line 18, in the definition of R11a and R12a, it is not clear what structural fragment is represented by the term "**pyrindolinyl**".
11. Claim 8 recites the limitation "or R11a and R12a taken together with the nitrogen atom to which they are attached form a cyclic radical chosen from pyrrolidyl, ... **indolinyl, pyrindolinyl, tetrahydroquinolyl, ... and naphthyridyl**" in lines 15-17. There is insufficient antecedent basis for this limitation in claim 1, in the definition of R11 and R12, which definition recites that 'or R11 and R12 taken together form 5- to 7-membered cyclic radical' and the above terms (i.e., indolinyl, etc.) are bicyclic groups having more than 7 ring members.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9, 12-50, 52-58, 62, 64, and 72-76 rejected under 35 U.S.C. 103(a) as being unpatentable over Poitout et al., WO 02/09090. (U.S. 6,759,415 belongs to the same patent family and is relied upon as the English equivalent of the WO document). The reference teaches a generic group of 2,4-imidiazolidinedione compounds, which embraces applicant's instantly claimed compounds. See formula (I) in page 3 wherein n is 0, and the compounds of Examples 1-572. The reference compounds are disclosed to be useful as pharmaceutical therapeutic agents for the treatment of arthritis, cancer, etc., see pages 19-20. The instant claims exclude reference disclosed compounds see the proviso statement a) in the claims. The instant claims, however, include compounds wherein one of Y and Y1 is $-O-CH_2-CF_3$; or one of R2 and R3 is imidazolylalkyl and the

other is alkyl, for example methyl (-CH_3); etc. Therefore, the instantly claimed compounds differ from the reference compounds by a -CH_2 group and it is well established that compounds that differ by a –CH_2 group are structural homologs. It would have been obvious to one having ordinary skill in the art at the time of the invention to modify the reference compounds to prepare the structural homolog. One having ordinary skill in the art would have been motivated to prepare the instantly claimed compounds because such structurally homologous compounds are expected to possess similar properties. It has been held that compounds that are structurally homologous to prior art compounds are *prima facie* obvious, absent a showing of unexpected results. *In re Hass*, 60 USPQ 544 (CCPA 1944); *In re Henze*, 85 USPQ 261 (CCPA 1950).

Allowable Subject Matter

Claim 62 is allowed. The references of record do not teach or fairly suggest the instantly claimed compounds.

Receipt is acknowledged of the Information Disclosure Statement filed on December 13, 2004 and a copy is enclosed herewith.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Tuesday-Friday from 6:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Deepak Rao
Primary Examiner
Art Unit 1624

October 30, 2006